



## **Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States**

Downloaded from <http://aidsinfo.nih.gov/guidelines> on 7/28/2012 EST.

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at <http://aidsinfo.nih.gov/e-news>.

## Mechanisms of Action of Antiretroviral Prophylaxis in Reducing Perinatal Transmission of HIV (Updated September 14, 2011)

### Panel's Recommendations

- Antiretroviral (ARV) drugs reduce perinatal transmission by several mechanisms, including lowering maternal antepartum viral load and providing infant pre- and post-exposure prophylaxis. Therefore, combined antepartum, intrapartum, and infant ARV prophylaxis is recommended to prevent perinatal transmission of HIV **(AI)**.

## Lessons from International Clinical Trials of Short-Course Antiretroviral Regimens for Prevention of Perinatal Transmission of HIV (Updated September 14, 2011)

### Panel's Recommendations

- All pregnant women who require therapy for their own health should receive a combination antepartum antiretroviral (ARV) drug regimen containing at least three drugs for treatment, which will also reduce the risk of perinatal transmission **(AI)**.
- Combination antepartum drug regimens are also recommended for prevention of perinatal transmission in women who do not yet require therapy for their own health **(AII)**.
- ARV prophylaxis is more effective when given for a longer than a shorter duration. Therefore, ARV drugs should be started as soon as possible in women who require treatment for their own health **(AI)**, and without delay after the first trimester in women who do not require immediate initiation of therapy for their own health, although earlier initiation can be considered in these women as well **(BIII)** (see [Recommendations for Use of Antiretroviral Drugs during Pregnancy](#)).
- In the absence of antepartum administration of ARV drugs, ARV drugs should be administered intrapartum in combination with infant ARV prophylaxis to reduce the risk of perinatal transmission (see [Intrapartum Care](#)) **(AI)**; if antepartum and intrapartum ARV drugs are not received, infant ARV prophylaxis should be provided (see [Infant Antiretroviral Prophylaxis](#)) **(AI)**.
- Adding single-dose intrapartum/newborn nevirapine to the standard antepartum combination ARV regimens used for prophylaxis or treatment in pregnant women in the United States is not recommended. This is because the drug does not appear to provide additional efficacy in reducing transmission and it may be associated with development of nevirapine resistance **(AI)**.
- Breastfeeding is not recommended for HIV-infected women in the United States—including those receiving combination antiretroviral therapy (ART)—because safe, affordable, and feasible alternatives are available **(AII)**.

## Perinatal Transmission of HIV and Maternal HIV RNA Copy Number (Updated September 14, 2011)

### Panel's Recommendations

- All HIV-infected pregnant women should be counseled about and administered antiretroviral (ARV) drugs during pregnancy for prevention of perinatal transmission, regardless of their HIV RNA levels **(AI)**.

## Preconception Counseling and Care for HIV-Infected Women of Childbearing Age (Updated September 14, 2011)

### Panel's Recommendations

- Discuss childbearing intentions with all women of childbearing age on an ongoing basis throughout the course of their care **(AIII)**.
- Include information about effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy **(AI)**.
- During preconception counseling include information on safer sexual practices and elimination of use of alcohol and illicit drugs, and smoking, which are important for the health of all women as well as for fetal/infant health, should pregnancy occur **(AII)**.
- When evaluating HIV-infected women, include assessment of HIV disease status and need for antiretroviral therapy (ART) for their own health **(AII)**.
- Choose an ART regimen for HIV-infected women of childbearing age based on consideration of effectiveness for treatment of maternal disease, teratogenic potential of the drugs in the regimen should pregnancy occur, and possible adverse outcomes for mother and fetus **(AII)**.

## Reproductive Options for HIV-Concordant and Serodiscordant Couples (Updated September 14, 2011)

### Panel's Recommendations

- For serodiscordant couples who want to conceive, expert consultation is recommended so that approaches can be tailored to specific needs, which may vary from couple to couple **(AIII)**.
- Partners should be screened and treated for genital tract infections before attempting to conceive **(AII)**.
- For an HIV-infected female with an HIV-uninfected male partner, the safest conception option is artificial insemination, including the option of self-insemination with her partner's sperm during the peri-ovulatory period **(AIII)**.
- For HIV-infected men with an HIV-uninfected female partner, the use of sperm preparation techniques coupled with either intrauterine insemination, in vitro fertilization, or intracytoplasmic sperm injection should be considered if using donor sperm from an HIV-uninfected male for insemination is unacceptable **(AII)**.
- In a serodiscordant couple who wishes to conceive, initiation of antiretroviral therapy (ART) for the HIV-infected partner is recommended if the infected partner has a CD4 count  $\leq 550$  cells/mm<sup>3</sup> **(AI)**. For HIV-infected individuals with CD4 counts  $>550$  cells/mm<sup>3</sup>, initiation of ART could be considered **(BIII)**. If therapy is initiated, maximal viral suppression is recommended before conception is attempted **(AIII)**.
- Data are insufficient at the current time to recommend peri-conception administration of antiretroviral (ARV) pre-exposure prophylaxis for HIV-uninfected partners to reduce the risk of sexual transmission **(AIII)**.

## Antepartum Care (Updated September 14, 2011)

### Panel's Recommendations

- Initial evaluation of infected pregnant women should include assessment of HIV disease status and recommendations regarding initiation of antiretroviral (ARV) drugs or the need for any modification if currently receiving antiretroviral therapy (ART) **(AIII)**. The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
- Regardless of plasma HIV RNA copy number or CD4 cell count, all pregnant HIV-infected women should receive a combination antepartum ARV drug regimen to prevent perinatal transmission **(AI)**. A combination regimen is recommended both for women who require therapy for their own health **(AI)** and for prevention of perinatal transmission in those who do not yet require therapy **(AII)**.
- The known benefits and potential risks of ARV use during pregnancy should be discussed with all women **(AIII)**.
- ARV drug-resistance studies should be performed before starting or modifying ARV drug regimens in women whose HIV RNA levels are above the threshold for resistance testing (e.g., >500 to 1,000 copies/mL) (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)) **(AI)**. When HIV is diagnosed late in pregnancy, ARV therapy or prophylaxis should be initiated pending results of resistance testing **(BIII)**.
- In counseling patients, the importance of adherence to the ARV regimen should be emphasized **(AII)**.
- Considerations regarding continuation of the ARV regimen for maternal therapeutic indications after delivery are the same as for nonpregnant individuals. The pros and cons of continuing versus discontinuing ARV drugs postpartum should be discussed with women so they can make educated decisions about postpartum ARV use before delivery **(AIII)**. Such decisions should be made in consultation with the provider who will assume responsibility for the women's HIV care going forward after delivery.
- Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and drug abuse treatment services, and public assistance programs is essential to ensure that infected women adhere to their ARV drug regimens **(AIII)**.

## HIV-Infected Pregnant Women Who Have Never Received Antiretroviral Drugs (Antiretroviral Naive) (Updated September 14, 2011)

### Panel's Recommendations

- HIV-infected pregnant women who meet standard criteria for initiation of antiretroviral therapy (ART) per adult antiretroviral (ARV) treatment guidelines should receive standard potent combination ART as recommended for nonpregnant adults, taking into account what is known about the use of specific drugs in pregnancy and the risk of teratogenicity ([Table 5](#)) (AI).
- For women who require immediate initiation of therapy for their own health, treatment should be started as soon as possible, including in the first trimester (AII). (Note that the use of efavirenz should be avoided during the first trimester.)
- A three-drug combination ARV regimen for prophylaxis of perinatal transmission also is recommended for HIV-infected pregnant women who do not require treatment for their own health (AII).
- Consideration can be given to delaying initiation of prophylaxis until after the first trimester (BIII) in women who are receiving ARV drugs solely for prevention of perinatal transmission, but earlier initiation of therapy may be more effective in reducing *in utero* transmission.
- ARV regimens should include a dual nucleoside reverse transcriptase inhibitor (NRTI) backbone that includes one or more NRTIs with high levels of transplacental passage, if possible, to provide pre-exposure prophylaxis to the infant (AIII).
- If HIV RNA is above the threshold for resistance testing (i.e., >500–1,000 copies/mL), ARV drug-resistance studies should be performed before starting the ARV drug regimen (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)) (AI). If HIV is diagnosed late in pregnancy, the ARV drug regimen should be initiated pending results of resistance testing (BIII).
- Nevirapine can be used as a component of the ARV drug regimen for pregnant women with CD4 cell counts  $\leq 250$  cells/mm<sup>3</sup>. In pregnant women with CD4 cell counts >250 cells/mm<sup>3</sup>, however, nevirapine should be used only if the benefit clearly outweighs the risk because the drug is associated with an increased risk of hepatic toxicity (AII).

## HIV-Infected Pregnant Women Who Are Currently Receiving Antiretroviral Treatment (Updated September 14, 2011)

### Panel's Recommendations

- In general, pregnant women receiving and tolerating an antiretroviral therapy (ART) regimen that is currently effective in suppressing viral replication should continue on the regimen; however, the use of efavirenz should be avoided in the first trimester (AIII).
- HIV antiretroviral (ARV) drug-resistance testing is recommended for pregnant women who have detectable viremia (e.g., >500–1,000 copies/mL) on therapy (see [Failure of Viral Suppression](#)) (AI).
- Pregnant women receiving and tolerating nevirapine-containing regimens who are virologically suppressed should continue the regimen, regardless of CD4 count (AIII).

## HIV-Infected Pregnant Women Who Have Previously Received Antiretroviral Treatment or Prophylaxis but Are Not Currently Receiving Any Antiretroviral Medications (Updated September 14, 2011)

### Panel's Recommendations

- Obtain an accurate history of all prior antiretroviral (ARV) regimens used for treatment of HIV disease or prevention of transmission, including virologic efficacy, tolerance to the medications, results of prior resistance testing, and any adherence issues **(AIII)**.
- If HIV RNA is above the threshold for resistance testing (e.g., >500–1,000 copies/mL), ARV drug-resistance studies should be performed before starting an ARV drug regimen (see [Antiretroviral Drug Resistance and Resistance Testing in Pregnancy](#)) **(AIII)**. In women who present late in pregnancy, therapy or prophylaxis should be initiated pending results of resistance testing **(BIII)**.
- Choose and initiate a combination ARV drug regimen based on results of resistance testing and prior history of antiretroviral therapy (ART) while avoiding drugs with teratogenic potential (efavirenz in the first trimester of pregnancy) or with known adverse potential for the mother **(AII)**.
- Consult specialists in treatment of HIV infection about the choice of ART in women who previously received ARVs for their own health **(AIII)**.
- Perform repeat ARV drug-resistance testing **(AI)**, assess adherence, and consult with an HIV treatment specialist to guide changes in ARV drugs in women do not achieve virologic suppression on their ARV regimens (see [Monitoring of the Woman and Fetus During Pregnancy](#)).

## Special Situations — HIV/Hepatitis B Virus Coinfection (Updated September 14, 2011)

### Panel's Recommendations

- Screening for hepatitis B virus (HBV) infection is recommended for all pregnant women who have not been screened during the current pregnancy **(AII)**.
- The HBV vaccine series should be administered to pregnant women who screen negative for hepatitis B (i.e., hepatitis B surface antigen negative, hepatitis B core antibody negative, and hepatitis B surface antibody negative) **(AII)**.
- Pregnant women with **chronic** HBV infection should be screened for antibodies to hepatitis A virus (HAV), and those who screen negative should receive the HAV vaccine series **(AII)**.
- Interferon alfa and pegylated interferon alfa are not recommended during pregnancy **(AIII)**.
- **The management of HIV/HBV coinfection in pregnancy is complex and** consultation with an expert in HIV and HBV is strongly recommended **(AIII)**.
- **All pregnant women with HIV/HBV coinfection should receive a combination antiretroviral (ARV) drug regimen, including a dual nucleoside reverse transcriptase inhibitor (NRTI)/nucleotide analogue reverse transcriptase inhibitor (NtRTI) backbone with two drugs active against both HIV and HBV (AII). Tenofovir plus lamivudine or emtricitabine is the preferred dual NRTI/NtRTI backbone of a combination antepartum ARV regimen in HIV/HBV-coinfected pregnant women (AI).**
- **If ARV drugs are discontinued postpartum in women with HIV/HBV coinfection, frequent monitoring of liver function tests for potential exacerbation of HBV infection is recommended, with prompt reinitiation of treatment for both HIV and HBV if a flare is suspected (BIII).**
- **Pregnant women with HIV/HBV coinfection receiving ARV drugs should be counseled about the signs and symptoms of liver toxicity, and liver transaminases should be assessed 1 month following initiation of ARV drugs and at least every 3 months thereafter (BIII).**
- Within 12 hours of birth, infants born to women with HBV infection should receive hepatitis B immune globulin (HBIG) and the first dose of the HBV vaccine series. The second and third doses of vaccine should be administered at ages 1 and 6 months, respectively **(AI)**.

## Special Situations — HIV/Hepatitis C Virus Coinfection (Updated September 14, 2011)

### Panel's Recommendations

- Screening for hepatitis C virus (HCV) infection is recommended for all HIV-infected pregnant women who have not been screened during the current pregnancy **(AIII)**.
- Interferon alfa and pegylated interferon alfa are not recommended and ribavirin is contraindicated during pregnancy **(AIII)**.
- Recommendations for antiretroviral (ARV) drug use during pregnancy are the same for women who have chronic HCV as for those without HIV/HCV coinfection **(BIII)**.
- Pregnant women with HIV/HCV coinfection receiving ARV drugs should be counseled about signs and symptoms of liver toxicity, and transaminases should be assessed **1 month** following initiation of ARV **drugs** and then **every 3 months** thereafter **(BIII)**.
- Decisions concerning mode of delivery in HIV/HCV-coinfected pregnant women should be based on **standard obstetric and HIV-related indications** alone **(see Intrapartum Care)** **(BIII)**.
- Infants born to women with HIV/HCV coinfection should be evaluated for HCV infection with **anti-HCV antibody testing after age 18 months (AII)**. Infants with a positive anti-HCV antibody should undergo confirmatory HCV RNA testing. If **earlier diagnosis is indicated or desired, HCV RNA virologic testing between ages 3 and 6 months can be performed (AIII)**.
- Women who are found to have chronic HCV infection should also be screened for hepatitis A virus (HAV) and hepatitis B virus (HBV) because they are at increased risk of complications from those two infections. Women with chronic HCV who are negative for hepatitis A immunoglobulin G (IgG) should receive the HAV vaccine series. If they are not infected with HBV (i.e., hepatitis B surface antigen negative, hepatitis B core antibody negative, and hepatitis B surface antibody negative), they should receive the HBV vaccine series **(AIII)**.



## Special Situations — HIV-2 Infection and Pregnancy (Updated September 14, 2011)

### Panel's Recommendations

- HIV-2 infection should be suspected in pregnant women who are from—or have partners from—countries in which the disease is endemic, who are HIV antibody positive on an initial enzyme-linked immunoassay screening test, and who have repeatedly indeterminate results on HIV-1 Western blot and an HIV-1 RNA viral load at or below the limit of detection **(BII)**.
- A regimen with two nucleoside reverse transcriptase inhibitors (NRTIs) and a boosted protease inhibitor (PI) currently is recommended for HIV-2-infected pregnant women who require treatment for their own health because they have significant clinical disease or CD4 counts  $<500$  cells/mm<sup>3</sup> **(AIII)**.
  - Based on available data on safety in pregnancy, zidovudine/lamivudine plus lopinavir/ritonavir would be preferred **(AIII)**. Tenofovir plus lamivudine or emtricitabine plus lopinavir/ritonavir can be considered as an alternative **(BIII)**.
- Optimal prophylactic regimens have not been defined for HIV-2-infected pregnant women who do not require treatment for their own health (i.e., CD4 counts  $\geq 500$  cells/mm<sup>3</sup> and no significant clinical disease). Experts have recommended the following approaches:
  - A boosted PI-based regimen (two NRTIs plus lopinavir/ritonavir) for prophylaxis, with the drugs stopped postpartum **(BIII)**;
  - Zidovudine prophylaxis alone during pregnancy and intrapartum **(BIII)**.
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and enfuvirtide are not active against HIV-2 and should not be used for treatment or prophylaxis **(AIII)**.
- All infants born to HIV-2-infected mothers should receive the standard 6-week zidovudine prophylactic regimen **(BIII)**.
- In the United States, breastfeeding is not recommended for infants of HIV-2-infected mothers **(AIII)**.

## Special Situations — Acute HIV Infection (Updated September 14, 2011)

### Panel's Recommendations

- When acute retroviral syndrome is suspected in pregnancy or during breastfeeding, a plasma HIV RNA test should be obtained in conjunction with an HIV antibody test (see [Identifying, Diagnosing, and Managing Acute HIV-1 Infection](#) in the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](#)) **(AII)**.
- Repeat HIV antibody testing in the third trimester is recommended for pregnant women with initial negative HIV antibody tests who are known to be at risk of HIV, are receiving care in facilities that have an HIV incidence in pregnant women of at least 1 per 1,000 per year, are incarcerated, or reside in jurisdictions with elevated rates of HIV infection (see [Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings](#)) **(AII)**.
- All pregnant women with acute or recent HIV infection should start a combination antiretroviral (ARV) drug regimen as soon as possible to prevent mother-to-child transmission, with the goal of suppressing plasma HIV RNA to below detectable levels **(AI)**.
- In women with acute HIV infection, baseline genotypic resistance testing should be performed simultaneously with initiation of the ARV regimen, and the ARV regimen should be adjusted, if necessary, to optimize virologic response **(AIII)**.
- Because clinically significant resistance to protease inhibitors (PIs) is less common than resistance to non-nucleoside reverse transcriptase inhibitors (NNRTIs) in ARV-naïve individuals in general, a ritonavir-boosted PI-based regimen should be initiated **(AIII)**.

## Special Situations — Stopping Antiretroviral Drugs during Pregnancy (Updated September 14, 2011)

### Panel's Recommendations

- HIV-infected women receiving antiretroviral treatment (ART) who present for care during the first trimester should continue treatment during pregnancy **(AII)**. Women who present in the first trimester on an efavirenz-containing regimen should continue on therapy without interruption but, when possible, an alternative antiretroviral (ARV) drug should be substituted for efavirenz **(AIII)**.
- If an ARV drug regimen is stopped acutely for severe or life-threatening toxicity, severe pregnancy-induced hyperemesis unresponsive to antiemetics, or other acute illnesses that preclude oral intake, all ARV drugs should be stopped and reinitiated at the same time **(AIII)**.
- If an ARV drug regimen is being stopped electively and the patient is receiving a non-nucleoside reverse transcriptase inhibitor (NNRTI) drug, consideration should be given to either: (1) stopping the NNRTI first and continuing the other ARV drugs for a period of time; or (2) switching from an NNRTI to a protease inhibitor (PI) before interruption and continuing the PI with the other ARV drugs for a period of time before electively stopping. The optimal interval between stopping an NNRTI and the other ARV drugs is unknown; at least 7 days is recommended. Given the potential for prolonged detectable efavirenz concentrations for more than 3 weeks in patients receiving efavirenz-based therapy, some experts recommend continuing the other ARV agents or substituting a PI plus two other agents for up to 30 days **(CIII)**.
- If nevirapine is stopped and more than 2 weeks have passed before restarting therapy, nevirapine should be restarted with the 2-week dose escalation period **(AII)**.

## Special Situations — Failure of Viral Suppression (Updated September 14, 2011)

### Panel's Recommendations

- If an ultrasensitive HIV RNA assay indicates failure of viral suppression to below detectable levels after an adequate period of treatment:
  - Assess resistance and adherence **(AII)**.
  - Consult an HIV treatment expert **(AIII)**.
- Scheduled cesarean delivery is recommended for HIV-infected pregnant women who have HIV RNA levels >1,000 copies/mL near the time of delivery **(AII)**.

## Monitoring of the Woman and Fetus During Pregnancy (Updated September 14, 2011)

### Panel's Recommendations

- CD4 cell count should be monitored at the initial antenatal visit **(AI)** and at least every 3 months during pregnancy **(BIII)**. Monitoring of CD4 count may be performed every 6 months in patients on antiretroviral treatment (ART) for more than 2–3 years who are adherent to therapy, clinically stable, and have sustained viral suppression **(BIII)**.
- Plasma HIV RNA levels should be monitored at the initial visit **(AI)**; 2–4 weeks after initiating (or changing) antiretroviral (ARV) drug regimens **(BI)**; monthly until RNA levels are undetectable **(BIII)**; and then at least every 3 months during pregnancy **(BIII)**. HIV RNA levels also should be assessed at approximately 34–36 weeks' gestation to inform decisions about mode of delivery (see [Transmission and Mode of Delivery](#)) **(AIII)**.
- Genotypic ARV drug-resistance testing should be performed at baseline in all HIV-infected pregnant women with HIV RNA levels >500–1,000 copies/mL, whether they are ARV-naïve or currently on therapy **(AIII)**. Repeat testing is indicated following initiation of an ARV regimen in women who have suboptimal viral suppression or who have persistent viral rebound to detectable levels after prior viral suppression on an ARV regimen **(AII)**.
- Monitoring for complications of ARV drugs during pregnancy should be based on what is known about the adverse effects of the drugs a woman is receiving **(AIII)**.
- First-trimester ultrasound is recommended to confirm gestational age and, if scheduled cesarean delivery is necessary, to guide timing of the procedure (see [Transmission and Mode of Delivery](#)) **(AII)**.
- Given the limited data on the effect of combination ARV drugs on the fetus, most experts would recommend second-trimester ultrasound to assess fetal anatomy for women who have received combination ARV regimens during the first trimester, particularly if the regimen included efavirenz **(BIII)**.
- In women on effective combination ARV regimens, no perinatal transmissions have been reported after amniocentesis, but a small risk of transmission cannot be ruled out. If amniocentesis is indicated in HIV-infected women, it should be done only after initiation of an effective combination ARV drug regimen and, if possible, when HIV RNA levels are undetectable **(BIII)**. In women with detectable HIV RNA levels in whom amniocentesis is deemed necessary, consultation with an expert should be considered.

## Pharmacokinetic Changes (Updated September 14, 2011)

### Panel's Recommendations

- Altered dosing during pregnancy may be required for some protease inhibitors (PIs), such as lopinavir/ritonavir (see [Table 5](#)) **(AII)**.

## Teratogenicity (Updated September 14, 2011)

### Panel's Recommendations

- All cases of antiretroviral (ARV) drug exposure during pregnancy should be reported to the Antiretroviral Pregnancy Registry (see details at <http://www.APRegistry.com>) **(AIII)**.
- Efavirenz should not be used in the first trimester and nonpregnant women receiving efavirenz should be counseled to avoid pregnancy **(AIII)**.

## Combination Antiretroviral Drug Regimens and Pregnancy Outcome (Updated September 14, 2011)

### Panel's Recommendations

- Clinicians should be aware of a possible small increased risk of preterm birth in pregnant women receiving protease-inhibitor (PI)-based combination antiretroviral (ARV) regimens; however, given the clear benefits of such regimens for both the women's health and the prevention of mother-to-child transmission, PIs should not be withheld for fear of altering pregnancy outcome **(AII)**.

## Nevirapine and Hepatic/Rash Toxicity (Updated September 14, 2011)

### Panel's Recommendations

- Nevirapine-based regimens should be initiated in women with CD4 counts  $>250$  cells/mm<sup>3</sup> only if the benefits clearly outweigh the risks because of the drug's potential for causing hepatic toxicity/hypersensitivity reaction **(AII)**.
- Women who become pregnant while receiving nevirapine-containing regimens and who are tolerating the regimen well can continue on the therapy regardless of CD4 count **(AII)**.

## Nucleoside Reverse Transcriptase Inhibitor Drugs and Mitochondrial Toxicity (Updated September 14, 2011)

### Panel's Recommendations

- The combination of stavudine and didanosine should not be prescribed during pregnancy due to reports of lactic acidosis and maternal/neonatal mortality with prolonged use in pregnancy **(AII)**.
- Mitochondrial dysfunction should be considered in uninfected children with perinatal exposure to antiretroviral (ARV) drugs who present with severe clinical findings of unknown etiology, particularly neurologic findings **(AII)**.
- Long-term clinical follow-up is recommended for any child with *in utero* exposure to ARV drugs **(AIII)**.

## Protease Inhibitor Therapy and Hyperglycemia (Updated September 14, 2011)

### Panel's Recommendations

- HIV-infected women taking antiretroviral (ARV) drug regimens during pregnancy should undergo glucose screening with a standard, 1-hour, 50-g glucose loading test at 24–28 weeks' gestation **(AIII)**. Some experts would perform earlier glucose screening in women receiving ongoing protease inhibitor (PI)-based regimens initiated before pregnancy, similar to recommendations for women with high-risk factors for glucose intolerance **(BIII)**.

## Antiretroviral Drug Resistance and Resistance Testing in Pregnancy (Updated September 14, 2011)

### Panel's Recommendations

- HIV drug-resistance testing is recommended for:
  - All pregnant women with HIV RNA levels above the threshold for resistance testing (e.g., >500–1,000 copies/mL) not currently receiving antiretroviral (ARV) drugs, before starting treatment or prophylaxis **(AIII)**.
  - All pregnant women receiving antenatal ARV drugs who have suboptimal viral suppression or persistent viral rebound to detectable levels after prior viral suppression on an ARV regimen **(AII)**.
- Empiric initiation of ARV drugs before results of resistance testing are available may be warranted, with adjustment as needed after the test results are available, for optimal prevention of perinatal transmission **(BIII)**.

## Management of Antiretroviral Drug Resistance during Pregnancy (Updated September 14, 2011)

### Panel's Recommendations

- Women who have documented zidovudine resistance and are on regimens that do not include zidovudine for their own health should still receive intravenous zidovudine during labor whenever possible, along with their established antiretroviral (ARV) regimens **(AII)**.
- In women who are receiving a stavudine-containing regimen, the drug should be discontinued during labor while intravenous zidovudine is being administered (see [Intrapartum Care](#)) **(AII)**.
- The optimal prophylactic regimen for newborns of women with ARV resistance is unknown (see [Infant Antiretroviral Prophylaxis](#)). Therefore, ARV prophylaxis for an infant born to a woman with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist, preferably before delivery **(AIII)**.

## Prevention of Antiretroviral Drug Resistance (Updated September 14, 2011)

### Panel's Recommendations

- HIV-infected pregnant women should be given combination antiretroviral (ARV) drug regimens to maximally suppress viral replication; that is the most effective strategy for preventing development of resistance and minimizing risk of perinatal transmission **(AII)**.
- All pregnant women should be counseled about the importance of adherence to prescribed ARV medications to reduce the potential for development of resistance **(AII)**.
- Pregnant women who are receiving a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combination ARV therapy solely for prophylaxis of transmission that will be discontinued after delivery should receive nucleoside analogue agents for at least 7 days after the NNRTI is stopped to minimize risk of resistance **(AI)**. An alternative strategy is to substitute a protease inhibitor (PI) for the NNRTI prior to the interruption and to continue the PI with dual nucleoside reverse transcriptase inhibitors (NRTIs) **for at least 7 days after stopping the NNRTI (CIII)**. The optimal interval between stopping an NNRTI and the other ARV drugs is not known (see [Stopping Antiretroviral Therapy during Pregnancy](#) and [Postpartum Follow-Up of HIV-Infected Women](#)).
- Adding single-dose maternal/infant nevirapine to an ongoing combination ARV regimen given for treatment or prophylaxis does not increase efficacy in reducing perinatal transmission and may result in nevirapine drug resistance in the mother and/or infant; therefore single-dose maternal/infant nevirapine is not recommended in this situation **(AI)**.

## Intrapartum Care (Updated September 14, 2011)

### Panel's Recommendations

- Intrapartum intravenous zidovudine is recommended for all HIV-infected pregnant women, regardless of their antepartum regimen, to reduce perinatal transmission of HIV **(AI)**.
- For women who are receiving a stavudine-containing antepartum regimen, stavudine should be discontinued during labor while intravenous zidovudine is being administered **(AI)**.
- Women who are receiving an antepartum combination antiretroviral (ARV) drug regimen should continue this regimen on schedule as much as possible during labor and before scheduled cesarean delivery **(AIII)**.
- Women receiving fixed-dose combination regimens that include zidovudine should receive intravenous zidovudine during labor while other oral ARV components are continued **(AIII)**.
- For women who have received antepartum ARV drugs but have suboptimal viral suppression near delivery (i.e., HIV RNA >1,000 copies/mL), scheduled cesarean delivery is recommended (see [Mode of Delivery](#)) **(AI)**. The addition of single-dose intrapartum/newborn nevirapine is not recommended **(AI)**.
- Women of unknown HIV status who present in labor should undergo rapid HIV antibody testing **(AII)**. If the results are positive, a confirmatory HIV test should be done as soon as possible and maternal/infant ARV drugs should be initiated pending results of the confirmatory test **(AII)**. If the confirmatory HIV test is positive, infant ARV drugs should be continued for 6 weeks (see [Neonatal Postnatal Care](#)) **(AI)**; if the test is negative, the infant ARV drugs should be stopped.
- Intravenous zidovudine is recommended for HIV-infected women in labor who have not received antepartum ARV drugs and infant combination ARV prophylaxis is recommended for 6 weeks (see [Infant Antiretroviral Prophylaxis](#)) **(AII)**.

## Transmission and Mode of Delivery (Updated September 14, 2011)

### Panel's Recommendations

- Scheduled cesarean delivery at 38 weeks' gestation is recommended for women with HIV RNA levels >1,000 copies/mL near the time of delivery, **irrespective of administration of** antepartum antiretroviral (ARV) drugs, and for women with unknown HIV RNA levels near the time of delivery **(AII)**.
- **Scheduled cesarean delivery is not routinely recommended** for prevention of perinatal transmission in pregnant women receiving combination ARV drugs with plasma HIV RNA levels <1,000 copies/mL near the time of delivery. Data **are insufficient to evaluate the potential benefit of cesarean delivery in this group, and** given the low rate of transmission in these patients, it is unclear whether scheduled cesarean delivery would confer additional benefit in reducing transmission. This decision should be individualized based on discussion between the obstetrician and the mother **(BII)**.
- It is not clear whether cesarean delivery after rupture of membranes or onset of labor provides benefit in preventing perinatal transmission. Management of women originally scheduled for cesarean delivery who present with ruptured membranes or in labor must be individualized based on duration of rupture, progress of labor, plasma HIV RNA level, current ARV regimen, and other clinical factors **(BII)**.
- Women should be informed of the risks associated with cesarean delivery; the risks to the woman should be balanced with potential benefits expected for the neonate **(AIII)**.

## Other Intrapartum Management Considerations (Updated September 14, 2011)

### Panel's Recommendations

- **Generally avoid artificial rupture of membranes unless there are clear obstetric indications** because of a potential increased risk of transmission **(BIII)**.
- Routine use of fetal scalp electrodes for fetal monitoring should be avoided in the setting of maternal HIV infection **unless there are clear obstetric indications (BIII)**.
- **Operative** delivery with forceps or a vacuum extractor and/or episiotomy **should be performed only if there are clear obstetric indications (BIII)**.
- The antiretroviral drug (ARV) regimen a woman is receiving should be taken into consideration when treating excessive postpartum bleeding resulting from uterine atony:
  - In women who are receiving a cytochrome P (CYP) 3A4 enzyme inhibitor such as a protease inhibitor (PI), methergine should only be used if no alternative treatments for postpartum hemorrhage are available and the need for pharmacologic treatment outweighs the risks. If methergine is used, it should be administered in the lowest effective dose for the shortest possible duration **(BIII)**.
  - In women who are receiving a CYP3A4 enzyme inducer such as nevirapine or efavirenz, additional uterotonic agents may be needed because of the potential for decreased methergine levels and inadequate treatment effect **(BIII)**.



## Postpartum Management (Updated September 14, 2011)

### Panel's Recommendations

- Contraceptive counseling should be included as a critical aspect of postpartum care **(AIII)**.
- Decisions about continuing antiretroviral (ARV) drugs after delivery should take into account current recommendations for initiation of antiretroviral therapy (ART), current and nadir CD4 cell counts and trajectory, HIV RNA levels, adherence issues, whether the woman has an HIV-uninfected sexual partner, and patient preference **(AIII)**.
- For women continuing ARV drugs postpartum, arrangements for new or continued supportive services should be made before hospital discharge because the immediate postpartum period poses unique challenges to adherence **(AII)**.
- Women with a positive rapid HIV antibody test during labor require comprehensive follow-up, including confirmation of HIV infection. If infection is confirmed, a full health assessment is warranted, including evaluation for associated medical conditions, counseling related to newly diagnosed HIV infection, and assessment of need for ART and opportunistic infection (OI) prophylaxis **(AII)**.

## Infants Born to Mothers with Unknown HIV Infection Status (Updated September 14, 2011)

### Panel's Recommendations

- For infants born to mothers with unknown HIV status, rapid HIV antibody testing of the mother and/or infant is recommended as soon as possible after birth, with **immediate** initiation of infant antiretroviral (ARV) prophylaxis (see **Infant Antiretroviral Prophylaxis**) if the rapid test is positive **(AII)**. In the setting of a positive test, standard antibody confirmatory testing such as a Western blot also should be performed on mothers (or their infants) as soon as possible. If the confirmatory test is negative, ARV prophylaxis can be discontinued **(AIII)**.
- If the HIV antibody confirmatory test is positive, a newborn HIV DNA polymerase chain reaction (PCR) should be obtained **(AIII)**.
- If the newborn HIV DNA PCR is positive, ARV prophylaxis should be discontinued and the infant promptly referred to a pediatric HIV specialist for confirmation of the diagnosis and treatment of HIV infection with standard combination antiretroviral therapy (ART) **(AI)**.



## Infant Antiretroviral Prophylaxis (Updated September 14, 2011)

### Panel's Recommendations

- The 6-week neonatal component of the zidovudine chemoprophylaxis regimen is recommended for all HIV-exposed neonates to reduce perinatal transmission of HIV **(AI)**.
- Zidovudine should be initiated as close to the time of birth as possible, preferably within 6–12 hours of delivery **(AII)**.
- The 6-week zidovudine prophylaxis regimen is recommended at gestational age-appropriate doses; zidovudine should be dosed differently for premature infants less than 35 weeks than for infants at least 35 weeks of age (see [Zidovudine Dosing](#) and [Table 8](#)) **(AII)**.
- In the United States, the use of antiretroviral (ARV) drugs other than zidovudine cannot be recommended in premature infants because of lack of dosing and safety data **(BIII)**.
- The use of intrapartum/neonatal zidovudine is recommended regardless of maternal history of zidovudine resistance **(BIII)**.
- Infants born to HIV-infected women who have not received antepartum ARV drugs should receive prophylaxis with a combination ARV drug regimen, begun as soon after birth as possible **(AI)**. A randomized, controlled trial has shown that a 2-drug regimen of zidovudine given for 6 weeks combined with three doses of nevirapine in the first week of life (at birth, 48 hours later, and 96 hours after the second dose) is as effective as but less toxic than a 3-drug regimen of zidovudine, nelfinavir and lamivudine. The 2-drug regimen is preferred due to lower toxicity and because nelfinavir powder is no longer available in the United States (see [General Considerations for Choice of Infant Prophylaxis](#) and [Table 9](#)) **(AI)**.
- In other scenarios, the decision to combine other drugs with the 6-week zidovudine regimen should be made in consultation with a pediatric HIV specialist, preferably before delivery, and should be accompanied by counseling of the mother on the potential risks and benefits of this approach **(BIII)**.
- The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV, including infant care.

## Initial Postnatal Management of the HIV-Exposed Neonate (Updated September 14, 2011)

### Panel's Recommendations

- A complete blood count (CBC) and differential should be performed on newborns as a baseline evaluation **(BIII)**.
- Decisions about the timing of subsequent monitoring of hematologic parameters in infants depend on baseline hematologic values, gestational age at birth, clinical condition of the infants, the zidovudine dose being administered, receipt of concomitant medications, and maternal antepartum therapy **(CIII)**.
- Some experts recommend more intensive monitoring of hematologic and serum chemistry and liver function assays **at birth and when diagnostic HIV polymerase chain reaction (PCR) tests are obtained** in infants exposed to combination antiretroviral (ARV) drug regimens *in utero* or during the neonatal period **(CIII)**.
- If hematologic abnormalities are identified in infants receiving prophylaxis, decisions on whether to continue infant ARV prophylaxis need to be individualized. Consultation with an expert in pediatric HIV infection is advised if discontinuation of prophylaxis is considered **(CIII)**.
- Routine measurement of serum lactate is not recommended. However, measurement can be considered if an infant develops severe clinical symptoms of unknown etiology (particularly neurologic symptoms) **(CIII)**.
- Virologic tests are required to diagnose HIV infection in infants <18 months of age and should be performed **within the first** 14–21 days of life, at 1–2 months, and at **4–6** months of age **(AII)**.
- To prevent *Pneumocystis jirovecii* pneumonia (PCP), all infants born to women with HIV infection should begin PCP prophylaxis at age 4–6 weeks, after completing their ARV prophylaxis regimen, unless there is adequate test information to presumptively exclude HIV infection (see [USPHS/IDSA Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and Infected Children](#)) **(AII)**.

## Long-Term Follow-Up of Antiretroviral Drug-Exposed Infants (Updated September 14, 2011)

### Panel's Recommendations

- Children with *in utero*/neonatal exposure to antiretroviral (ARV) drugs who develop significant organ system abnormalities of unknown etiology, particularly of the nervous system or heart, should be evaluated for potential mitochondrial dysfunction **(CIII)**.
- Follow-up of children with exposure to ARVs should continue into adulthood because of the theoretical concerns regarding the potential for carcinogenicity of nucleoside analogue ARV drugs **(CIII)**.